AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-3. (cancelled)

4. (currently amended) A method for ~~in vitro inserting~~ *in vitro* insertion of a nucleic acid of interest initially included in a DNA vector, within a predetermined target nucleotide sequence present in a chromosome contained in a prokaryotic or eukaryotic cell, ~~characterized in that it~~said method comprises ~~the following steps of~~:

a) contacting the DNA vector comprising the nucleic acid of interest, and replicating said DNA vector in said prokaryotic or eukaryotic cell, with a mutagenic agent blocking the DNA replication in the cell;

b) transfecting said prokaryotic or eukaryotic ~~cells~~ cells with the DNA vector ~~such as~~ obtained at the end of step a); and

c) selecting ~~the~~ prokaryotic or eukaryotic cells for which the nucleic acid of interest has been integrated into the predetermined target nucleotide sequence.

5. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that it further comprises the~~ further comprising ~~following step of:~~

~~d)~~ selecting~~, amongst~~ from the prokaryotic or eukaryotic cells ~~as selected~~ obtained in step c), the cells wherein the DNA vector sequences, other than those of the nucleic acid of interest, were removed.

6. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the mutagenic agent is selected ~~amongst~~ from the group consisting of: N-acetoxy-2-acetylaminofluorene (N-AcO-AAF), an alkylating agent, benzo(a) pyrene-diol-epoxyde (BPDE) ~~as well as a~~and UV irradiation.

7. (currently amended) ~~A~~ The method according to claim 5, ~~characterized in that~~ wherein the mutagenic agent is N-acetoxy-2-acetylaminofluorene (N-AcO-AAF).

8. (currently amended) ~~A~~ The method according to claim 7, ~~characterized in that~~ wherein in step a), the N-AcO-AAF is contacted with the DNA vector comprising the nucleic acid of interest, at a concentration adapted for binding at least 10 N-AcO-AAF molecules per molecule of the polynucleotide.

9. (currently amended) ~~A~~ The method according to claim 8, ~~characterized in that~~ wherein the concentration ~~in~~ of N-AcO-AAF is adapted for binding at least 50 N-AcO-AAF molecules per molecule of the polynucleotide.

10. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the nucleic acid of interest to be inserted into the ~~genome~~ chromosome of the prokaryotic or eukaryotic cell, being initially included in said DNA vector comprises respectively at its ~~end~~ 5' terminus and at its ~~end~~ 3' terminus, sequences ~~with a high identity degree~~having at least 99.5% identity with the corresponding sequences located at the ~~ends~~ 5' terminus and 3' terminus of the target DNA contained in the chromosome.

11. (currently amended) ~~A~~ The method according to claim 10, ~~characterized in that~~ wherein the sequences respectively located at ~~end~~ the 5' terminus and at ~~end~~ 3' terminus of the nucleic acid of interest are identical respectively to the ~~ends~~ 5' terminus and 3' terminus of the target DNA contained in the chromosome.

12. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the nucleic acid of interest included in said DNA vector comprises a selection marker nucleotide sequence.

13. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the nucleic acid of interest comprises an open reading frame ~~coding~~ that encodes a protein of therapeutic interest.

14. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the nucleic acid of interest comprises an open reading frame disrupted by a heterologous nucleotide sequence.

15. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the nucleic acid of interest ~~codes~~ encodes an antisense RNA.

16. (currently amended) ~~A~~ The method according to claim 13, ~~characterized in that~~ wherein the nucleic acid of interest further comprises a nucleotide sequence with a promoter function, being functional in the selected prokaryotic or eukaryotic host cell, under the control of which the open reading frame or the sequence ~~coding~~ encoding the RNA included in said nucleic acid of interest is operably arranged.

17. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the ~~polynucleotide~~ nucleic acid

comprising the nucleic acid of interest comprises a marker nucleotide sequence located, in said polynucleotide, outside the nucleotide sequence of the nucleic acid of interest.

18. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein said DNA vector is a bacterial plasmid.

19. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein said DNA vector is a functional plasmid ~~being functional~~ in bacterial cells.

20. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein said DNA vector is a functional plasmid ~~being functional~~ in human cells.

21. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the DNA vector is a double strand linear DNA.

22. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the cells transfected in step b) comprise bacterial cells.

23. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the cells transfected in step b) consist ~~in~~ of non human mammalian cells.

24. (currently amended) ~~A~~ The method according to claim 4, ~~characterized in that~~ wherein the cells transfected in step b) consist ~~in~~ of human cells.